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CORRELATION BETWEEN SEVERITY OF DIABETIC RETINOPATHY AND HBA1C LEVEL IN PATIENTS WITH TYPE 2 DIABETIC MELLITUS IN A TERTIARY HEALTH CARE CENTRE: AN OBSERVATIONAL STUDY

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ABSTRACT

Aim: To correlate the levels of HBA1C with severity of diabetic retinopathy according to ETDRS classification.

Materials and methods: This is a cross-sectional, observational, descriptive study was conducted at major tertiary health care centre. Total 223 patients of type 2 Diabetes Mellitus (DM) with Diabetic Retinopathy (DR) studied for 1 year.

Results: Correlation between Hba1c levels and the severity of diabetic retinopathy was found to be statistically significant (p value < 0.05). Out of 223 cases, 139 were males, 84 were females. Hba1c levels were less 8% in 57 cases, 8-9.9 % in 83 cases while Hba1c levels were more than 10% in 83 cases. According to ETDRS classification 9 cases were very mild NPDR, 62 cases of mild NPDR, 45 cases of moderate NPDR, 32 cases of severe NPDR, 13 cases of very severe NPDR, 26 cases of mild PDR, 20 cases of high risk PDR and 16 cases of advanced eye disease.

Conclusion: There is a strong correlation between Hba1c levels, duration of DM and severity of DR. Hba1c can be used as a useful tool to assess long term control of DM and hence development of DR. Early treatment of DR is important to prevent this irreversible blindness.

KEYWORDS: Diabetic Retinopathy, HBA1C Levels, Diabetes Mellitus, ETDRS Classification

INTRODUCTION

The human eye is one of the most remarkable sensory organ systems. The eyes are peripheral organs for vision which function like a camera. (1) Blindness is a major public health problem in India as well as worldwide. According to WHO blindness is curable or preventable in approximately 80% of cases. (2) Previous studies done by various authors from the India reported avoidable blindness ranging from 80-95%. (3-4). Diabetes Mellitus (DM) is fifth leading cause of blindness worldwide. One of the major reasons of visual impairment and blindness among the diabetic patients is Diabetic Retinopathy (DR). As per statistics of 2013, diabetes-related retinal disease has affected approximately 382 million people globally, and it is expected to cross the number of 592 million by 2025. (5)

Diabetic retinopathy (DR) is one of most common microvascular complication of diabetes, especially type 2 Diabetes Mellitus. (6-7) Visual loss from diabetic retinopathy results from new vessels growth on the retina known as proliferative retinopathy. In addition, retinal blood vessels growth on the retina known a proliferative retinopathy. In addition, retinal blood vessels can become leaky resulting in swelling of the centre of the retina, called macular oedema. Proliferative retinopathy, severe non-proliferative retinopathy and clinically significant macular oedema are considered as sight threatening retinopathy.(6) A Survey on diabetic retinopathy was conducted in twenty-one district of India in which the prevalence of diabetic retinopathy among diabetics was 16.99%, prevalence of sight threatening diabetic retinopathy was 3.6% and that of mild retinopathy was 11.8%.(8) The most effective therapy for diabetic retinopathy is “prevention”.(18) Early detection and treatment of diabetics as well as ophthalmologic complications arising from diabetes superadded with timely intervention can result in prevention of visual impairment and blindness thus improving the quality of life.(7-11)

Glycated haemoglobin (Hba1c) reflects the chronic blood glucose concentration. Hba1c is a convenient and reducible tool and the standardized Hba1c assay is not inferior to the blood glucose assay. (10,12). In January 2010, the American Diabetes Association (ADA) published revised criteria for the diagnosis of diabetes mellitus which stated Hba1c value of 48

mmol/mol (6.5%) or more is diagnostic of diabetes mellitus. (10,13) Hba1c can help diabetic individual in deterrence of microvascular complications especially diabetic retinopathy. (13)

Studies done by various authors have established strong relationship between Hba1c and diabetic retinopathy. Furthermore Lind et al. (14) stated that the risk of retinopathy was low if Hba1c levels were below 6.5% and risk increased with higher Hba1c levels, thus highlighting the role of Hba1c in the clinical correlation of severity of diabetic retinopathy.

MATERIALS AND METHODS

It was a cross section, observational, descriptive study in department of ophthalmology in tertiary health care centre, India for 1 year duration with convenience sampling method. Outpatient department paper and investigation report of patients attending outpatient department ophthalmology with consent was source of data.

We excluded from the study patients with type I diabetes mellitus, gestational diabetes mellitus, diabetic patient without retinopathy, patients on long term steroids (derange sugar level), patients with dense cataracts and corneal opacities which prevented visualization of posterior segment, patients with pre-existing non diabetic maculopathy (like due to serous retinopathy, age related macular degeneration, drug induced, other macular degeneration, other ocular infections.) and presence of factors affecting Hba1c value (example- Known case of renal diseases, chronic kidney disease, on dialysis, diabetic patients with haemoglobinopathy).

Informed, written consent was taken from all patients before enrolment, after explaining to the patients in details the procedures in a language best understood by them. Data was collected on case record form and entered in excel sheet for statistical analysis. The data was collected with help of a customized proforma which was designed for the purpose of this study. The data was entered into a Microsoft excel sheet for calculations. Total 223 patients were studied with formula n= Z2p(100-p)/L2

RESULT

In this present study, majority cases belonged to age group 61-70 years i.e., 84(37.67%) cases followed by age group 51-60 years which included 78 (34.98%) cases. Least number of cases belonged to the age group 81-90 years i.e., 1 (0.45%) case. The age ranged from 41 years to 82 years with mean 59.48 years. Out of 223 cases, 139 (62.33%) were males, 84 (37.67%) were females. The male to female ratio was 1.65:1. Table 1 and 2 highlights distribution of cases according to the age and sex respectively.

101 patients had history of clinically diagnosed diabetes since less than 5 years. 88 patients had duration of diabetes ranging from 6 to 10 years. Duration of diabetes was more than 10 years in 34 patients. Out of 223 cases, Hba1c levels were less than 8% in 57 cases (25.56%), 8 TO 9.9% in 83 cases (37.22%) while Hba1c levels were more than or equal to 10% in 83 cases (37.22%)

Grading of diabetic retinopathy according to Early Treatment Diabetic Retinopathy Study (ETDRS) classification revealed 9 cases (4.04%) of very mild Non Proliferative Diabetic Retinopathy (NPDR), 62cases (27.80%) of mild NPDR (Fig. 1-A), 45 cases (2.18%) of moderate NPDR and 32 cases (14.35%) of severe NPDR (Fig. 1-B), 13 cases (5.83%) of very severe NPDR, 26 cases (11.66%) of mild Proliferative Diabetic Retinopathy (PDR)(Fig. 1-C), 20 cases (8.97%) of high risk PDR and 16 cases (7.17%) of advanced eye disease (Fig. 1-D). Patients with very mild NPDR had mean Hba1c value of 7.57% and average duration of diabetes mellitus was 5.4 years. Patients with mild NPDR had mean Hba1c value 7.97% and average duration of diabetes mellitus was 5.4 years. Patients with moderate NPDR had mean Hba1c value of 9.02% and average duration of DM was 6.2 years. Patients with severe NPDR had mean Hba1c value of 10.79% and average duration of DM was 8.3 years. Cases with mild PDR had mean Hba1c value of 10.42% and average duration of DM was 8.6 years. Cases with high-risk PDR had mean Hba1c value of 10.68% and average duration of DM was 8.4 years. Cases with Advanced Eye Disease (AED) had mean Hba1c value of 9.96% and average duration of DM was 10.6 years. Table 3 highlights the distribution of cases according to the grading of diabetic retinopathy with their average Hba1c levels and average duration of diabetes mellitus.

Table 4 highlights p value by comparison of Hba1c values by unpaired T test. Hba1c values of cases with very mild NPDR when compared with Hba1c values of cases with mild NPDR, moderate NPDR, severe NPDR, very severe NPDR, mild PDR, high risk PDR and AED shows significant (p value < 0.05). Hba1c values of cases with mild NPDR when compared with Hba1c values of cases with moderate NPDR shows significant difference (p value < 0.05). Hba1c values of cases with moderate NPDR as well as severe NPDR when compared with Hba1c values of cases with very severe NPDR, mild PDR and high-risk PDR shows significant difference (p value < 0.05).

19 patients of 223 cases revealed presence of diabetic macular oedema of which 15 cases had advanced eye disease while 2 cases had mild PDR and 2 cases had high risk PDR. Hba1c values ranged from 7.0 – 15.3% with mean value of 10.56%.

DISCUSSION

This study describes study of Hba1c levels in patients with diabetic retinopathy along with its correlation with severity of diabetic retinopathy according to ETDRS classification and helps to established pivotal role of Hba1c to determine severity of diabetic retinopathy reflecting the importance of strict glycaemic control in type 2 DM patients to prevent microvascular complications especially diabetic retinopathy.

In the present study, the age group ranged from 41 to 82 years. The mean age was 59.48 years. Majority of the cases were in the age group 61-70 years (37.67% cases). Followed by age group 51-60 years (34.98% cases). In the similar study done by Vashist P et al (8), author recorded highest prevalence of diabetic retinopathy in the 60 – 69 years age group. Lokesh

S et al (15) included 50 patients of type 2 diabetic mellitus with visual impairment in their study and found out that most common age group affected with diabetic retinopathy was 61 – 70 years. Bukke SN et al (16) in their study of 100 diabetic patients reported majority of patients affected DR were between 61-70 years of age. Other similar studies done by A Tanuja et al (17) and Raman R et al (18) revealed that most commonly affected age group was 51 to 60 years and 50 to 59 years respectively however, both these studies found that age group 61 – 70 years was second most commonly affected.

In this study, we found that males more commonly affected than females. The male to female ratio was 1.65:1. Similar results were seen in studies done by Vashist P et al (8), A. Tanuja et al (17), Lokesh S et al (15), Bukke SN et al (16), Raman R et al (18). All these studies revealed that males were more commonly affected than females.

Out of total 223 cases, 101 patients (45.29%) had history of clinically diagnosed diabetes since less than 5 years. 88 patients (39.46%) had duration of diabetes ranging from 6 to 10 years. Duration of diabetes was more than 10 years in 34 patients (15.25%). Hba1c levels were less than 8% in 57 cases (25.56%), 8 to 9.9% in 83 cases (37.22%) while Hba1c levels were more than or equal to 10% in 83 cases (37.22%). Chronic glycaemia is the important causative factor leading to complications of diabetes mellitus. The Diabetes Control and Complications Trials (DCCT) demonstrated that improvement of glycaemic control reduced incidence of both non proliferative and proliferative retinopathy significantly. These benefits of an improvement in glycaemic control at any Hba1c level is beneficial. (9,21) The UKPDS demonstrated that reduction in Hba1c by one percentage point was associated with a 35% reduction in microvascular complications. (9)

In this study, it was observed that mean Hba1c value and mean duration of DM was lower for patients with milder grades of DR as compared to patients with severe grades of DR and higher Hba1c value associated with severe DR. CURES Eye study (19) reported that 41.8 percent cases had DR after 15 years of diabetes. Longer duration of diabetes was associated with proportional increase in severity of DR. For every five-year increase in the duration of diabetes, the risk for DR increased by 1.89 times. Bukke SN et al (16) in their study of 100 diabetic patients with DR showed a significant association between the duration of DM and severity of DR. The patients having longer duration of DM (> 10 years) had either very severe NPDR or PDR and vice versa. Raman R et al (18) published a large study in 2014 which included 13,079 participants and reported that in patients with diabetes of more than 15 years duration, higher proportions of them had all types of DR. Similar results were seen in study conducted by Lokesh S et al (15) which included fifty patients of type 2 diabetes mellitus with blurring of vision. Study results revealed that severe forms of DR were more commonly associated with higher Hba1c and milder form of DR were more in patients with Hba1c less than 10.0%. They concluded that increase in Hba1c levels increases frequency as well as severity of diabetic retinopathy. In Barbodose eye study, Leske et al (20) found that with every 1% increase in Hba1c from baseline value, risk of DR increases more than 2-fold. Lind et al (14) in their recent study evaluated 10,398 patients and stated that the risk of retinopathy was low if Hba1c levels were below 6.5% and higher Hba1c levels were associated with increased risk of retinopathy. Studies done by various other authors have established strong relationship between Hba1c and DR.

CONCLUSION

There is a strong correlation between Hba1c levels, duration of DM and severity of DR. Hba1c can be used as a useful tool to assess long term control of DM and hence development of DR. Early treatment of DR is important to prevent this irreversible blindness. Severe grades of diabetic retinopathy manifested in patients with higher levels of Hba1c. Hence, strict glycaemic control and reduction in the Hba1c concentration in diabetic patients can reduce the severity of diabetic retinopathy thus improving quality of life of diabetic patients. Effective strategies for prevention, early diagnosis and treatment need to be planned and implemented to tackle the huge burden of diabetes blindness.

N = 223

Age (in Years)	Number of Cases	Percentage
41-50	42	18.83%
51-60	78	34.98%
61-70	84	37.67%
71-80	18	8.07%
81-90	01	0.45%
TOTAL	223	100%

Table No.1: Shows distribution of cases according to the age

N = 223

Sex	Female	Male	Total
Number of Cases	84	139	223
Percentage	37.67%	62.33%	100%

Table No.2: Shows distribution of cases according to the sex

N = 223

Grading of diabetic retinopathy	Number of cases	Range of Hba1c (%)	Mean Hba1c +/- S.D. (%)	Mean duration of DM (Years)
Very mild NPDR	9 (4.04%)	5.6 - 11.1	7.57 +/- 1.80	5.4
Mild NPDR	62 (27.80%)	5.3 – 11.1	7.97 +/- 1.50	5.4
Moderate NPDR	45 (20.18%)	6 – 14.5	9.02 +/- 1.72	6.2
Severe NPDR	32 (14.35%)	6.6 – 12.6	9.44 +/- 1.67	7.3
Very Severe NPDR	13 (5.83%)	8.5 - 13	10.76 +/- 1.40	8.3

Mild PDR	26 (11.66%)	6.2 – 13.2	10.42 +/- 1.83	8.6
High Risk PDR	20 (8.97%)	6.5 – 15.3	10.68 +/- 2.25	8.4
Adavnced Eye Disease	16 (7.17%)	7 – 14.3	9.96 +/- 2.21	10.6

Table No.3: Shows distribution of cases according to the grading of diabetic retinopathy with their average Hba1c Levels and average duration of Diabetes Mellitus

N = 223

Grading of Diabetic Retinopathy	**Very mild NPDR**	**Mild NPDR**	**Moderate NPDR**	**Severe NPDR**	**Very severe NPDR**	**Mild PDR**	**High risk PDR**	**Advanced eye disease**
Very mild NPDR	-	0.463	0.025	0.006	0.0001	0.0002	0.001	0.011
Mild NPDR	-	-	0.001	3.84	3.52	4.19	2.65	5.9
Moderate NPDR	-	-	-	0.29	0.001	0.002	0.002	0.089
Severe NPDR	-	-	-	-	0.016	0.038	0.027	0.371
Very severe NPDR	-	-	-	-	-	0.556	0.908	0.264
Mild PDR	-	-	-	-	-	-	0.666	0.465
High risk PDR	-	-	-	-	-	-		0.34
Advanced eye disease	-	-	-	-	-	-	-	-

Table No. 4: Shows p value by comparison of Hba1c values (Mean +/- Sd) by unpaired T test. p value of less than 0.05 is statistically significant

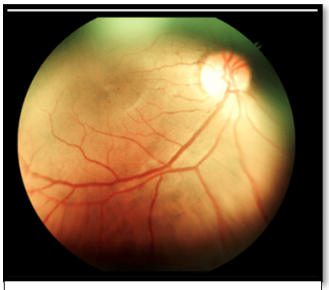

Fig.1-A) Fundus photograph showing microaneurysms (Mild NPDR)

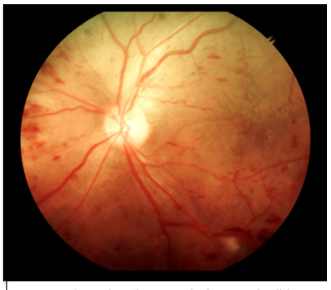

Fig.1- B) Fundus photograph showing dot/blot haemorrhages with cotton wool spot (Moderate to Severe NPDR)

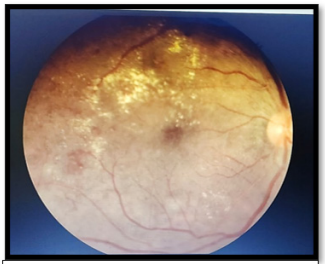

Fig. 1-C) Fundus photograph showing Proliferative Diabetic Retinopathy

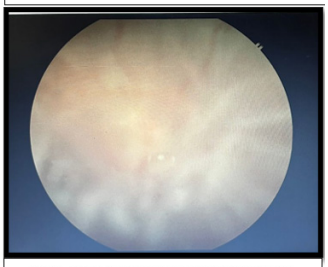

Fig. 1-D) Fundus photograph showing retinal detachment (Advanced Eye Disease)

Legends of Images

Fig.1-A) Fundus photograph showing microaneurysms (Mild NPDR)

Fig.1- B) Fundus photograph showing dot/blot haemorrhages with cotton wool spot (Moderate to Severe NPDR)

Fig. 1-C) Fundus photograph showing Proliferative Diabetic Retinopathy

Fig. 1-D) Fundus photograph showing retinal detachment (Advanced Eye Disease)

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